

***Amendments to the Claims***

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (original) A method of treating hypersecretion of mucus, comprising administering, topically to the airways of a patient in need thereof, a therapeutically effective amount of a compound, said compound comprising:-

- (a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain;
- (b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and
- (c) a translocating domain that translocates the L-chain or L-chain fragment into the target cell;

with the proviso that said compound is not a botulinum toxin; and wherein, following administration to said patient, the compound binds to and delivers the L-chain or L-chain fragment into said target cell, thereby (i) inhibiting mucus secretion by mucus secreting cells, (ii) inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion, or (iii) inhibiting mucus secretion by mucus secreting cells and inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion.

2. (original) A method according to Claim 1, wherein said translocating domain is a translocating domain of a microbial protein.

3. (original) A method according to Claim 1, wherein said translocating domain is a translocating domain of a bacterial or viral protein.

4. (original) A method according to Claim 1, wherein said translocating domain is a translocating domain of a bacterial toxin, or a translocating domain of a

virally expressed membrane fusion protein.

5. (currently amended) ~~A method according to Claim 1, A method of treating hypersecretion of mucus, comprising administering, topically to the airways of a patient in need thereof, a therapeutically effective amount of a compound, said compound comprising:-~~

(a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain;

(b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and

(c) a translocating domain that translocates the L-chain or L-chain fragment into the target cell, wherein said translocating domain is selected from the group consisting of a translocating domain of clostridial neurotoxin, a translocating domain of diphtheria toxin, domain II of pseudomonas exotoxin A, a translocating domain of influenza virus haemagglutinin, a translocating domain of a fusogenic protein of Semliki Forest virus, a translocating domain of vesicular stomatitis virus glycoprotein G, a translocating domain of SER virus F protein and a translocating domain of Foamy virus envelope glycoprotein;

with the proviso that said compound is not a botulinum toxin; and wherein, following administration to said patient, the compound binds to and delivers the L-chain or L-chain fragment into said target cell, thereby (i) inhibiting mucus secretion by mucus secreting cells, (ii) inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion, or (iii) inhibiting mucus secretion by mucus secreting cells and inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion.

6. (original) A method according to Claim 1, wherein the targeting domain is a domain selected from the group consisting of Substance P, vasoactive intestinal polypeptide (VIP), beta<sub>2</sub> adrenoreceptor agonists, gastrin releasing peptide, and

calcitonin gene related peptide.

7. (original) A method according to Claim 1, wherein said targeting domain binds to a target cell selected from the group consisting of epithelial goblet cells, submucosal gland mucus-secreting cells, Clara cells, serous cells, sensory efferent C-fibres, and Non-adrenergic Non-Cholinergic neural system fibres.

8. (original) A method of treating chronic obstructive pulmonary disease (COPD), comprising administering, topically to the airways of a patient in need thereof, a therapeutically effective amount of a compound, said compound comprising:-

(a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain;

(b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and

(c) a translocating domain of that translocates the L-chain or L-chain fragment into the target cell;

with the proviso that said compound is not a botulinum toxin; and

wherein following administration to said patient the compound binds to and delivers the L-chain or L-chain fragment into said target cell, thereby (i) inhibiting mucus secretion by mucus secreting cells, (ii) inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion, or (iii) inhibiting mucus secretion by mucus secreting cells and inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion.

9. (original) A method according to Claim 8, wherein said translocating domain is a translocating domain of a microbial protein.

10. (original) A method according to Claim 8, wherein said translocating domain is a translocating domain of a bacterial or viral protein.

11. (original) A method according to Claim 8, wherein said translocating domain is a translocating domain of a bacterial toxin, or a translocating domain of a virally expressed membrane fusion protein.

12. (original) A method according to Claim 8, wherein said translocating domain is selected from the group consisting of a translocating domain of diphtheria toxin, domain II of pseudomonas exotoxin A, a translocating domain of influenza virus haemagglutinin, a translocating domain of a fusogenic protein of Semliki Forest virus, a translocating domain of vesicular stomatitis virus glycoprotein G, a translocating domain of SER virus F protein and a translocating domain of Foamy virus envelope glycoprotein.

13. (original) A method according to Claim 8, wherein the targeting domain is a domain selected from the group consisting of Substance P, VIP, beta<sub>2</sub> adrenoreceptor agonists, gastrin releasing peptide, and calcitonin gene related peptide.

14. (original) A method according to Claim 8, wherein said targeting domain selectively binds to a target cell selected from the group consisting of epithelial goblet cells, submucosal gland mucus-secreting cells, Clara cells, and serous cells.

15. (original) A method for treating asthma, comprising administering, topically to the airways of a patient in need thereof, a therapeutically effective amount of a compound, said compound comprising:-

- (a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain;
- (b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and
- (c) a translocating domain that translocates the L-chain or L-chain fragment

into the target cell;  
with the proviso that said compound is not a botulinum toxin; and  
wherein following administration to said patient the compound binds to and delivers the L-chain or L-chain fragment into said target cell, thereby (i) inhibiting mucus secretion by mucus secreting cells, (ii) inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion, or (iii) inhibiting mucus secretion by mucus secreting cells and inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion.

16. (original) A method according to Claim 15, wherein said translocating domain is a translocating domain of a microbial protein.

17. (original) A method according to Claim 15, wherein said translocating domain is a translocating domain of a bacterial or viral protein.

18. (original) A method according to Claim 15, wherein said translocating domain is a translocating domain of a bacterial toxin, or a translocating domain of a virally expressed membrane fusion protein.

19. (original) A method according to Claim 15, wherein said translocating domain is selected from the group consisting of a translocating domain of diphtheria toxin, domain II of pseudomonas exotoxin A, a translocating domain of influenza virus haemagglutinin, a translocating domain of a fusogenic protein of Semliki Forest virus, a translocating domain of vesicular stomatitis virus glycoprotein G, a translocating domain of SER virus F protein and a translocating domain of Foamy virus envelope glycoprotein.

20. (original) A method according to Claim 15, wherein the targeting domain is a domain selected from the group consisting of Substance P, VIP, beta<sub>2</sub> adrenoreceptor agonists, gastrin releasing peptide, and calcitonin gene related peptide.

21. (original) A method according to Claim 15, wherein said targeting domain selectively binds to a target cell selected from the group consisting of epithelial goblet cells, submucosal gland mucus-secreting cells, Clara cells, and serous cells.

22.-54. (cancelled)